Product Description SALSA® MLPA® Probemix P168-D1 ARVC-PKP2

To be used with the MLPA General Protocol.

Version D1. As compared to version C2, five reference probes have been replaced and one *DSP* probe has been removed. For complete product history see page 8.

Catalogue numbers:
- **P168-025R:** SALSA MLPA Probemix P168 ARVC-PKP2, 25 reactions.
- **P168-050R:** SALSA MLPA Probemix P168 ARVC-PKP2, 50 reactions.
- **P168-100R:** SALSA MLPA Probemix P168 ARVC-PKP2, 100 reactions.

To be used in combination with a SALSA MLPA reagent kit and Coffalyser.Net data analysis software. MLPA reagent kits are either provided with FAM or Cy5.0 dye-labelled PCR primer, suitable for Applied Biosystems and Beckman/SCIEX capillary sequencers, respectively (see www.mlpa.com).

Certificate of Analysis: Information regarding storage conditions, quality tests, and a sample electropherogram from the current sales lot is available at www.mlpa.com.

Precautions and warnings: For professional use only. Always consult the most recent product description AND the MLPA General Protocol before use: www.mlpa.com. It is the responsibility of the user to be aware of the latest scientific knowledge of the application before drawing any conclusions from findings generated with this product.

General information: The SALSA MLPA Probemix P168 ARVC-PKP2 is a **research use only (RUO)** assay for the detection of deletions or duplications in the *PKP2, DSG2, DSC2*, *JUP, DSP, TGFB3,* and *RYR2* genes*,* which are associated with Arrhythmogenic right ventricular cardiomyopathy (ARVC).

ARVC is a disease with primarily right ventricular dysplasia and is characterised by fibro-fatty infiltration of the myocardium. The clinical presentation is irregular but predominantly characterised by ventricular arrhythmias, syncope, and sudden cardiac death. Diagnosis can be difficult in certain cases but is facilitated by criteria proposed by the Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) Task Force.

Mutations in the plakophilin-2 (*PKP2*) gene have been found in approximately 30% of patients with ARVC. Other genes that have been linked to ARVC are desmoglein-2 (*DSG2*), desmoscollin-2 (*DSC2*), plakoglobin (*JUP*), desmoplakin (*DSP*), transforming growth factor-ß3 (*TGFB3*), and the cardiac ryanodine receptor (*RYR2*) genes. Mutations in one of these latter genes are found in only a small subset of ARVC patients.

More information is available at https://www.ncbi.nlm.nih.gov/books/NBK1131/.

This SALSA MLPA Probemix is not CE/FDA registered for use in diagnostic procedures. Purchase of this product includes a limited license for research purposes.

Gene structure and transcript variants:
Entrez Gene shows transcript variants of each gene: http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene
For NM_ mRNA reference sequences: http://www.ncbi.nlm.nih.gov/sites/entrez?db=nucleotide
Locus Reference Genomic (LRG) database: http://www.lrg-sequence.org/

Exon numbering: The *PKP2, DSG2, DSC2*, *JUP, DSP, TGFB3,* and *RYR2* exon numbering used in this P168-D1 ARVC-PKP2 product description is the exon numbering from the RefSeq transcript NM_004572.3, NM_001943.3, NM_004949.3, NM_002230.2, NM_004415.2, NM_003239.2, and NM_001035.3 which are identical to the LRG_398, LRG_397, LRG_400, LRG_401, LRG_423, LRG_399, and LRG_402 sequence. The exon numbering and NM_ sequence used have been retrieved on 07/2020. As changes to the NCBI database can occur after release of this product description, exon numbering may not be up-to-date.

Probemix content: The SALSA MLPA Probemix P168-D1 ARVC-PKP2 contains 44 MLPA probes with amplification products between 124 and 490 nucleotides (nt). This includes 16 probes for *PKP2* gene, one probe for each exon, with the exception of exon 2, including one in the promoter region, one probe in intron 1 and two probes for exon 4. Furthermore, five probes for *DSP* gene, three probes for *JUP*, *DSC2*, *DSG2* and *TGFB3* genes, and two probes for *RYR2* gene are included. In addition, nine reference probes are included that detect autosomal chromosomal locations. Complete probe sequences and the identity of the genes detected by the reference probes are available online (www.mlpa.com).

This probemix contains nine quality control fragments generating amplification products between 64 and 105 nt: four DNA Quantity fragments (Q-fragments), two DNA Denaturation fragments (D-fragments), one Benchmark fragment, and one chromosome X and one chromosome Y-specific fragment (see table below). More information on how to interpret observations on these control fragments can be found in the MLPA General Protocol and online at www.mlpa.com.

Length (nt)	Name
64-70-76-82	Q-fragments (only visible with <100 ng sample DNA)
88-96	D-fragments (low signal of 88 nt and 96 nt fragment indicates incomplete denaturation)
92	Benchmark fragment
100	X-fragment (X chromosome specific)
105	Y-fragment (Y chromosome specific)

MLPA technique: The principles of the MLPA technique (Schouten et al. 2002) are described in the MLPA General Protocol (www.mlpa.com).

MLPA technique validation: Internal validation of the MLPA technique using 16 DNA samples from healthy individuals is required, in particular when using MLPA for the first time, or when changing the sample handling procedure, DNA extraction method or instruments used. This validation experiment should result in a standard deviation ≤0.10 for all probes over the experiment.

Required specimens: Extracted DNA free from impurities known to affect MLPA reactions. For more information please refer to the section on DNA sample treatment found in the MLPA General Protocol.

Reference samples: A sufficient number (≥3) of reference samples should be included in each MLPA experiment for data normalisation. All samples tested, including reference DNA samples, should be derived from the same tissue type, handled using the same procedure, and prepared using the same DNA extraction method when possible. Reference samples should be derived from unrelated individuals who are from families without a history of arrhythmogenic right ventricular cardiomyopathy. More information regarding the selection and use of reference samples can be found in the MLPA General Protocol.

Positive control DNA samples: MRC-Holland cannot provide positive DNA samples. Inclusion of a positive sample in each experiment is recommended. Coriell Institute (https://catalog.coriell.org) and Leibniz Institute DSMZ (https://www.dsmz.de/home.html) have a diverse collection of biological resources which may be used as a positive control DNA sample in your MLPA experiments. The quality of cell lines can change; therefore samples should be validated before use.

Data analysis: Coffalyser.Net software should be used for data analysis in combination with the appropriate lot-specific MLPA Coffalyser sheet. For both, the latest version should be used. Coffalyser.Net software is freely downloadable at www.mlpa.com. Use of other non-proprietary software may lead to inconclusive or false results. For more details on MLPA quality control and data analysis, including normalisation, see the Coffalyser.Net Reference Manual.

Interpretation of results: The standard deviation of each individual probe over all the reference samples should be ≤0.10 and the dosage quotient (DQ) of each individual reference probe in the patient samples should be between 0.80 and 1.20. When these criteria are fulfilled, the following cut-off values for the DQ of the probes can be used to interpret MLPA results for autosomal chromosomes or pseudo-autosomal regions:

Copy number status	Dosage quotient
Normal	0.80 < DQ < 1.20
Homozygous deletion	DQ = 0
Heterozygous deletion	0.40 < DQ < 0.65
Heterozygous duplication	1.30 < DQ < 1.65
Heterozygous triplication/Homozygous duplication	1.75 < DQ < 2.15
Ambiguous copy number	All other values

- Arranging probes according to chromosomal location facilitates interpretation of the results and may reveal more subtle changes such as those observed in mosaic cases. Analysis of parental samples may be necessary for correct interpretation of complex results.
- False positive results: Please note that abnormalities detected by a single probe (or multiple consecutive probes) still have a considerable chance of being a false positive result. Incomplete DNA denaturation (e.g. due to salt contamination) can lead to a decreased probe signal, in particular for probes located in or near a GC-rich region. The use of an additional purification step or an alternative DNA extraction method may resolve such cases. Additionally, contamination of DNA samples with cDNA or PCR amplicons of individual exons can lead to an increased probe signal (Varga et al. 2012). Analysis of an independently collected secondary DNA sample can exclude these kinds of contamination artefacts.
- Normal copy number variation in healthy individuals is described in the database of genomic variants: http://dgv.tcag.ca/dgv/app/home. Users should always consult the latest update of the database and scientific literature when interpreting their findings.
- Not all abnormalities detected by MLPA are pathogenic. In some genes, intragenic deletions are known that result in very mild or no disease (as described for *DMD* by Schwartz et al. 2007). For many genes, more than one transcript variant exists. Copy number changes of exons that are not present in all transcript variants may not have clinical significance. Duplications that include the first or last exon of a gene (e.g. exons 1-3) might not result in inactivation of that gene copy.
- Copy number changes detected by reference probes or flanking probes are unlikely to have any relation to the condition tested for.
- When running MLPA products, the capillary electrophoresis protocol may need optimization. False results can be obtained if one or more peaks are off-scale. For example, a duplication of one or more exons can be obscured when peaks are off-scale, resulting in a false negative result. The risk on off-scale peaks is higher when probemixes are used that contain a relatively low number of probes. Coffalyser.Net software warns for off-scale peaks while other software does not. If one or more peaks are off-scale, rerun the PCR products using either: lower injection voltage / injection time settings, or a reduced amount of sample by diluting PCR products.

Limitations of the procedure:

- In most populations, the major cause of genetic defects in the *PKP2, DSG2, DSC2*, *JUP, DSP, TGFB3,* and *RYR2* genes are small (point) mutations, most of which will not be detected by using SALSA MLPA Probemix P168 ARVC-PKP2.
- MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect copy number neutral inversions or translocations. Even when MLPA did not detect any aberrations, the possibility remains that biological changes in that gene or chromosomal region *do* exist but remain undetected.
- Sequence changes (e.g. SNPs, point mutations, small indels) in the target sequence detected by a probe can cause false positive results. Mutations/SNPs (even when >20 nt from the probe ligation site) can reduce the probe signal by preventing ligation of the probe oligonucleotides or by destabilising the binding of a probe oligonucleotide to the sample DNA.

Confirmation of results: Copy number changes detected by only a single probe always require confirmation by another method. An apparent deletion detected by a single probe can be due to e.g. a mutation/polymorphism that prevents ligation or destabilises the binding of probe oligonucleotides to the DNA sample. Sequence analysis can establish whether mutations or polymorphisms are present in the probe target sequence. The finding of a heterozygous mutation or polymorphism indicates that two different alleles of the sequence are present in the sample DNA and that a false positive MLPA result was obtained.

Copy number changes detected by more than one consecutive probe should be confirmed by another independent technique such as long range PCR, qPCR, array CGH or Southern blotting, whenever possible. Deletions/duplications of more than 50 kb in length can often be confirmed by FISH.

ARVC mutation database: www.arvcdatabase.info. We strongly encourage users to deposit positive results in the ARVD/C Genetic Variants Database. Recommendations for the nomenclature to describe deletions/duplications of one or more exons can be found on http://varnomen.hgvs.org/.

Please report copy number changes detected by the reference probes, false positive results due to SNPs and unusual results (e.g., a duplication of *PKP2* exons 5 and 7 but not exon 6) to MRC-Holland: info@mlpa.com.

Table 1. SALSA MLPA Probemix P168-D1 ARVC-PKP2

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]							
		Reference	PKP2	DSG2	DSP	TGFB3	DSC2	JUP	RYR2
64-105	Control fragments – see table in probemix content section for more information								
124 *	Reference probe 19616-L26275	4p13							
130	**DSG2 probe** 15483-L17323			**Exon 1**					
136	**DSC2 probe** 15484-L23210						**Exon 1**		
142	**PKP2 probe** 05383-L04780		**Promoter**						
151	**PKP2 probe** 05391-L24225		**Exon 8**						
160	**TGFB3 probe** 05414-L04824					**Exon 1**			
166	Reference probe 09106-L09165	4q25							
172	**PKP2 probe** 18562-L23895		**Exon 1**						
179 Ж	**PKP2 probe** 18376-SP0649-L23341		**Exon 9**						
188	**DSP probe** 05418-L24226				**Exon 5**				
196	**JUP probe** 14866-L16590							**Exon 2**	
202	**PKP2 probe** 05385-L24227		**Intron 1**						
209	**PKP2 probe** 20990-L29416		**Exon 10**						
218	**DSP probe** 05419-L24229				**Exon 7**				
226	**DSG2 probe** 15486-L24230			**Exon 15**					
232	**DSC2 probe** 15487-L17327						**Exon 7**		
238	**PKP2 probe** 05386-L04783		**Exon 3**						
244	Reference probe 17871-L22130	2p21							
251	**DSP probe** 18377-L29417				**Exon 1**				
265	**TGFB3 probe** 05415-L04825					**Exon 6**			
274 *	Reference probe 19294-L30901	10q23							
282	**PKP2 probe** 05387-L04784		**Exon 4**						
288	**PKP2 probe** 15488-L18692		**Exon 6**						
295	**PKP2 probe** 18378-L24231		**Exon 12**						
301	**RYR2 probe** 05935-L04837								**Exon 3**
310	**DSP probe** 05936-L04831				**Exon 21**				
319 *	Reference probe 16274-L18566	20q11							
328	**PKP2 probe** 05388-L04785		**Exon 5**						
339	**PKP2 probe** 05396-L24232		**Exon 13**						
352	**RYR2 probe** 05428-L04838								**Exon 97**
361	Reference probe 08674-L08686	9q31							
373	**DSC2 probe** 15489-L17329						**Exon 17**		
384	**PKP2 probe** 05397-L29419		**Exon 14**						
391	**DSP probe** 05423-L04833				**Exon 24**				
401	**TGFB3 probe** 14865-L16589					**Exon 7**			
409 *	Reference probe 21338-L29744	3p14							
421 +	**PKP2 probe** 05390-L24235		**Exon 7**						
427	**PKP2 probe** 05411-L08911		**Exon 4**						
436	**JUP probe** 05426-L24236							**Exon 12**	
445	Reference probe 12002-L23932	8q13							
454	**JUP probe** 05937-L04835							**Exon 9**	
463	**PKP2 probe** 18379-L23434		**Exon 11**						
481	**DSG2 probe** 15490-L17330			**Exon 6**					
490 *	Reference probe 19137-L25693	21q22							

* New in version D1.

\+ SNP rs146882581 and/or rs147240502 could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.

Ж This probe consists of three parts and has two ligation sites. A low signal of this probe can be due to depurination of the sample DNA, e.g. due to insufficient buffering capacity or a prolonged denaturation time. When this occurs in reference samples, it can look like an increased signal in the test samples.

a) See above section on exon numbering for more information.

Table 2. P168-D1 probes arranged according to chromosomal location

Table 2a. *PKP2* gene

Length (nt)	SALSA MLPA probe	PKP2 exon[a]	Ligation site NM_004572.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*116-118 (Exon 1)*		
142	05383-L04780	Promoter	1485 nt before exon 1	ATGGTTGGATGT-TTCCACCTGGCT	2.0 kb
172	18562-L23895	Exon 1	131 nt after exon 1	CTCGCCGTCTTC-GGTATGACCGAC	15.8 kb
202	05385-L24227	Intron 1	1504 nt before exon 2	GATGGAGCATAG-AGGTTGATTTCC	2.3 kb
238	05386-L04783	Exon 3	763-764	CACTTTGACACA-TACCACAGACAG	9.2 kb
427 #	05411-L08911	Exon 4	1185-1186	GGAGCGAGCAGT-GAGTATGCTCGA	0.1 kb
282	05387-L04784	Exon 4	1277-1278	AATCTGAAGCTC-GGAAGAGGGTGA	18.1 kb
328 #	05388-L04785	Exon 5	1382-1383	TGAGAAACTTAG-TATTTGAAGACA	7.5 kb
288	15488-L18692	Exon 6	45 nt before exon 6	CTGTGTTCATAA-AGGAGCCTGCCC	2.2 kb
421 +	05390-L24235	Exon 7	1708-1709	ACGGAGAATATC-ATCATCCCCTTT	17.0 kb
151 #	05391-L24225	Exon 8	1856-1857	GAAGATGTGACG-GACTCATTGACT	1.6 kb
179 Ж	18376-SP0649-L23341	Exon 9	2019-2018; 1980-1979 reverse	TCTGGATATTCC-39 nt spanning oligo-GCTCTGCCTCCA	1.1 kb
209	20990-L29416	Exon 10	2191-2192	TTGATCGCCAAA-AGTGTCCGCAAC	18.9 kb
463 #	18379-L23434	Exon 11	2327-2328	CCCGAAAGATGC-TGCATGTTGGTG	6.5 kb
295	18378-L24231	Exon 12	136 nt after exon 12	AGCCAGGCCAGA-TCATCTGGTCAG	3.3 kb
339 #	05396-L24232	Exon 13	2674-2675	CACACGGAACTG-CATCATGCCTAC	0.4 kb
384	05397-L29419	Exon 14	2903-2904	CCAGAAAACAAA-TAGAACATAATT	
		stop codon	*2759-2761 (Exon 14)*		

Table 2b. *RYR2* gene

Length (nt)	SALSA MLPA probe	RYR2 exon[a]	Ligation site NM_001035.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*339-341 (Exon 1)*		
301	05935-L04837	Exon 3	538-539	CATCTGCACCTT-TGTGCTGGAGCA	467.2 kb
352	05428-L04838	Exon 97	14368-14369	CAAGGCAGCTCT-GGACTTCAGTGA	
		stop codon	*15240-15242 (Exon 105)*		

Table 2c. *DSP* gene

Length (nt)	SALSA MLPA probe	DSP exon[a]	Ligation site NM_004415.4	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*246-248 (Exon 1)*		
251	18377-L29417	Exon 1	278-277, reverse	CCCAGAGTGTTG-ATCCGCGGGTGG	20.7 kb
188	05418-L24226	Exon 5	856-857	GGAGATGGACAT-GGTGGCCTGGGG	2.7 kb
218	05419-L24229	Exon 7	1063-1064	GCGACAGCTGCA-GAACATCATTCA	2.0 kb
310	05936-L04831	Exon 21	3148-3149	GCTGGCCTCATA-CACCTCAGGACT	8.0 kb
391	05423-L04833	Exon 24	8794-8795	GAGAGGAAGCTT-TGACGCCACAGG	
		stop codon	*8859-8861 (Exon 24)*		

Table 2d. *TGFB3* gene

Length (nt)	SALSA MLPA probe	TGFβ3 exon[a]	Ligation site NM_003239.4	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*1130-1132 (Exon 1)*		
160	05414-L04824	Exon 1	1411-1412	TGCACCCAGGAA-AACACCGAGTCG	19.6 kb
265	05415-L04825	Exon 6	2138-2139	TCCATGAACCTA-AGGGCTACTATG	2.2 kb
401	14865-L16589	Exon 7	2773-2774	CTGAGGTTGGAT-TTGCTCATTGCT	
		stop codon	*2366-2368 (Exon 7)*		

Table 2e. *JUP* gene

Length (nt)	SALSA MLPA probe	JUP exon[a]	Ligation site NM_002230.4	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*133-135 (Exon 2)*		
196	14866-L16590	Exon 2	166-167	AGCAGCCTATCA-AGGTGACTGAGT	13.0 kb
454	05937-L04835	Exon 9	1729-1730	AACTGCTGGTGA-AGGCCCACCAGG	1.3 kb
436	05426-L24236	Exon 12	2152-2153	ACTCCCTCTTCA-AGCATGACCCGG	
		stop codon	*2368-2370 (Exon 14)*		

Table 2f. *DSC2* gene

Length (nt)	SALSA MLPA probe	DSC2 exon[a]	Ligation site NM_004949.5	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*451-453 (Exon 1)*		
136	15484-L23210	Exon 1	271-272	AAAGCCCCTTGG-ATGAGAGGCAGG	15.5 kb
232	15487-L17327	Exon 7	1292-1293	CACACGCCTGAA-GTACTCCATCAT	18.8 kb
373	15489-L17329	Exon 17	3321-3322	TCATTATTTGGA-TGGAATCTCTTT	
		stop codon	*2992-2994 (Exon 16)*		

Table 2g. *DSG2* gene

Length (nt)	SALSA MLPA probe	DSG2 exon[a]	Ligation site NM_001943.5	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*76-78 (Exon 1)*		
130	15483-L17323	Exon 1	3 nt after exon 1	CTTCTCCTGGTA-AGTGCCGCAAGC	23.9 kb
481	15490-L17330	Exon 6	696-697	GAGCCTGCTTAT-CCTCCAGTGTTC	24.1 kb
226	15486-L24230	Exon 15	3002-3003	TACCTTGGTAGA-TCAGCCTTATGC	
		stop codon	*3430-3432 (Exon 15)*		

This probe's specificity relies on a single nucleotide difference compared to a related gene or pseudogene. As a result, an apparent duplication of only this probe can be the result of a non-significant single nucleotide sequence change in the related gene or pseudogene.
+ SNP rs146882581 and/or rs147240502 could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.
Ж This probe consists of three parts and has two ligation sites. A low signal of this probe can be due to depurination of the sample DNA, e.g. due to insufficient buffering capacity or a prolonged denaturation time. When this occurs in reference samples, it can look like an increased signal in the test samples.

a) See above section on exon numbering for more information.

b) Only partial probe sequences are shown. Complete probe sequences are available at www.mlpa.com. Please notify us of any mistakes: info@mlpa.com.

References

- Schouten JP et al. (2002). Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. *Nucleic Acids Res.* 30:e57.
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- Kjærgaard KA et al. (2016). Failure of ICD therapy in lethal arrhythmogenic right ventricular cardiomyopathy type 5 caused by the TMEM43 p. Ser358Leu mutation. *HeartRhythm Case Rep,* 2(3), 217.
- Mégarbané A et al. (2020). Homozygous deletion of exons 2–7 within TGFB3 gene in a child with severe Loeys-Dietz syndrome and Marfan-like features. *Am J Med Genet A*, 182(5), 1230-1235.
- Ozawa J et al. (2018). Differential Diagnosis Between Catecholaminergic Polymorphic Ventricular Tachycardia and Long QT Syndrome Type 1—Modified Schwartz Score—. *Circ J*, 82(9), 2269-2276.

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- Robyns T et al. (2017). Repeat genetic testing with targeted capture sequencing in primary arrhythmia syndrome and cardiomyopathy. *Eur J Hum Genet*, 25(12), 1313-1323.
- Sonoda K et al. (2017). Quantitative analysis of PKP2 and neighbouring genes in a patient with arrhythmogenic right ventricular cardiomyopathy caused by heterozygous PKP2 deletion. *EP Europace*, 19(4), 644-650.

P168 Product history	
Version	*Modification*
D1	Five reference probes have been replaced and one *DSP* probe has been removed.
C2	One reference probe was added and the length of several probes has been adjusted.
C1	New probes for exons 1, 9, 11 and 12 of the *PKP2* gene and exon 1 of the *DSP* gene have been included. Furthermore, two reference probes have been replaced.
B1	Several new reference probes and probes for *DSC2* and *DSG2* genes have been added. In addition, new control fragments have been included (QDX2).
A1	First release.

Implemented changes in the product description

Version D1-01 — 27 July 2020 (02P)
- Product description rewritten and adapted to a new template.
- Product description adapted to a new product version (version number changed, changes in Table 1 and Table 2).
- *TGFß3* gene renamed to *TGFB3* gene.
- 202 nt *PKP2* probe renamed from exon 2 to intron 1 as the ligation site of the probe is located 1504 nt before exon 2.
- Ligation sites of the probes targeting the *DSG2, DSC2*, *JUP, DSP, TGFB3,* and *RYR2* genes updated according to new version of the NM_ reference sequence.
- Warning added to Table 2 for probe specificity relying on a single nucleotide difference between target gene and related gene or pseudogene.

Version 11 (55) – 25 July 2016
- Product description adapted to a new product version (version number changed, lot number added, changes in Table 1 and Table 2, new picture included).
- Ligation sites of the probes targeting the *DSP*, *TFGß3*, *DSC2* and *DSG2* genes updated according to new version of the NM_reference sequence.
- Manufacturer's address adjusted.
- New references added on page 1.

Version 10 (54) – 13 March 2015
- New sample picture included in product description
- "Peak area" replaced with "peak height".
- Updated link for "Database of Genomic Variants".
- ARVC/D abbreviation explained on Page 1.

Version 09 (49)
- Product description adapted to a new product version (version number changed, lot number added, small changes in Table 1 and Table 2, new picture included).

More information: www.mlpa.com; www.mlpa.eu	
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